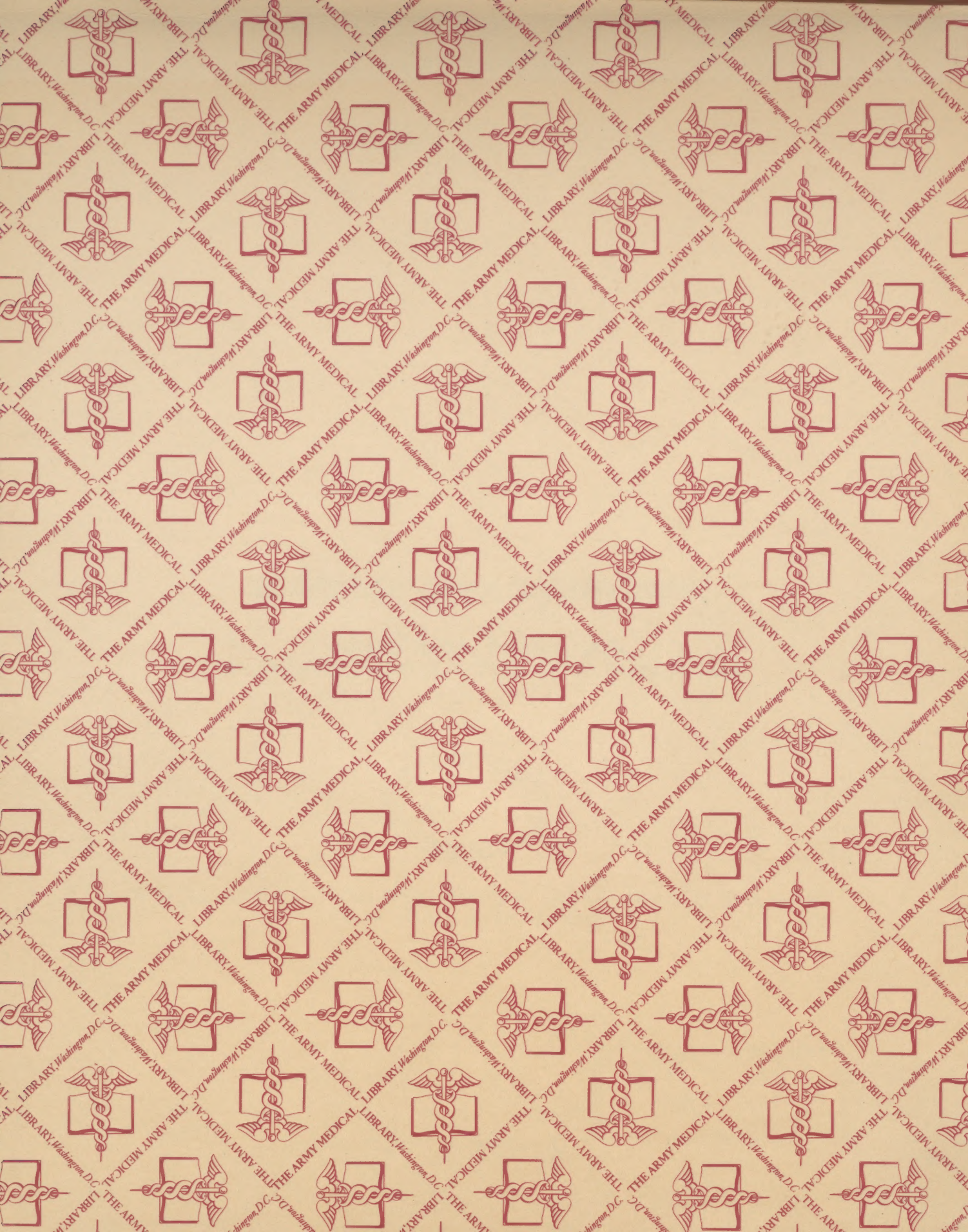
U. S. ARMY. OFFICE OF THE CHIEF SURGEON
EUROPEAN THEATRE OF OPERATIONS

DERMATOLOGIC ASPECTS OF CHEMICAL WARFARE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~~R E S T R I C T E D~~

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A.P.O. 871

THE DERMATOLOGIC ASPECTS OF CHEMICAL WARFARE

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With approval of Professional Services and Gas Casualty Divisions
Office of the Chief Surgeon

~~R E S T R I C T E D~~

The movement of large amounts of a poisonous gas to the Ypres front by the Germans in April 1915 was discovered and reported by Army Intelligence. Why this warning was unheeded is unknown. What happened thereafter is history that every military man knows. The lessons learned were tragic and only by a stroke of luck for the Allies, the Germans did not push their advantage. Immediately protective measures were evolved and since that time it has been "nip and tuck" between development of agents and development of protective measures to combat these agents.

Chemical Agents are divided into various categories. For our purpose they may be classified as:

1. Lung Irritants (Choking Gases)
2. Vesicants (Blister Gases)
3. Lacrimators (Tear Gases)
4. Irritant Smokes or Sternutators
5. Systemic Poisons
6. Screening Smokes and Incendiaries

The dermatologist is naturally most concerned with the vesicants, although some of the other agents will produce lesions of the skin when encountered in the liquid or solid form.

Not only do the classical blister gases affect the skin, but they have ophthalmological and systemic effects when the vapor or liquid reaches the eye, lungs or gastro-intestinal tract. Systemic effects may even be manifest by absorption from the skin alone.

In order that subsequent discussions are comprehensible a short discussion of the anatomy, chemistry and physiology of human skin is included here.

The human skin is one of the largest organs of the body. It must not be looked upon as a structure floating in space with no connections with underlying or internal structures. As a matter of fact, the skin and its appendages are intimately connected with all functions, organs and structures in the human body. The converse is also true.

The skin and its appendages (hair, nails, sweat and sebaceous glands) are the buffers between the outer world and the inner organs. The skin is admirably suited for its role as a protective agent against the onslaughts of the environment and as a heat regulating and excretory organ.

The structure which is characteristic for skin is the epidermis and its derivatives (hair and nails, sweat and sebaceous glands), while the cutis contains structures found elsewhere in the body (blood vessels, nerves and connective tissue). It is true that some of the nerve endings and corpuscles are found only in the skin (Pacinian, Meissner).

The epidermis consists of the basal cell layer (stratum malpigii) consisting of a single layer of cuboidal cells and is the layer from which the epidermis is proliferated. Thus, active proliferation occurs only in the basal cell layer. Extending up from the basal cell layer is the prickle cell layer (stratum mucosum), consisting of lighter staining (with Haematoxylin and eosin) stellate cells (squamous cells), each containing numerous projections (spines, prickles). These projections unite with those from adjacent cells and form protoplasmic bridges joining the cells. The spaces between the bridges thus united form lymph channels

so that each cell is surrounded by lymph. As the surface is approached the prickle cells begin to flatten and near the surface form the granular layer (stratum granulosum) containing flattened cells with deep staining nuclei and perinuclear granules (eleidin). On the palms and soles this is topped by a clear translucent layer in which the cells contain no nuclei (stratum lucidum). The outer layer of skin is the stratum corneum, consisting of flat, cornified, dead cells without nuclei, containing keratin. The stratum corneum is constantly being cast off and replaced by a new layer. Thus, proliferation occurs in the basal cell layer and extending upward to the stratum corneum one sees pictured the death of the cell.

The basal area of the epidermis in most places is thrown up into folds. The downward projections of the epidermis are the rete mucosum (rete pegs). The upward projections of the cutis locking into the epidermis are the papillary bodies.

The cutis consists mainly of fibrous (white) connective tissue (demonstrated by special stains), nerves, special nerve end organs, blood vessels, lymph spaces and vessels, sweat glands, sebaceous glands and hair follicles. The papillary bodies contain capillaries and nerves, and it is from here that nutrition is supplied to the avascular epidermis.

The subcutis contains larger nerves and blood vessels, connective tissue and fat. Sweat glands are also found here.

From the physiological point of view, it must be remembered that the epidermis is avascular and contains no nerve elements. Any agent acting primarily on the epidermis will, therefore, result in delayed clinical signs, cause little or no pain and present no vascular responses (erythema and edema) until later. Whereas, an agent which has great penetrability and is capable of regularly penetrating the intact epidermis to the cutis, will cause early vascular dilatation (erythema), edema, perivascular cellular exudate and/or infiltrate and sensory disturbances. Regardless of however easily the agent is able to penetrate the epithelial barrier and exert its effects on the structures of the cutis, the injury caused in the epidermis results in delayed symptoms. The typical epidermal response to irritation is intra (hydrops) and intercellular edema. Other than death no other primary local response is possible since there are no blood vessels and nerves. Should the toxic agent exert a great effect, the accumulation of fluid between the cells (in the intercellular spaces) increases and can be detected on microscopic examination, revealing dilatation of these spaces. The tissue is now becoming "waterlogged" (spongiotic). Increased accumulation of fluid results in the rupture of some of the intercellular bridges and fusion of adjacent spaces results in frank tiny blisters (vesicles). Fusion of these small vesicles results in the formation of large blisters (bullae). It must again be stressed that the blistering is localized to the epidermis and necessarily is delayed in onset because of the anatomy of the epidermis. In part this is due to the fact that the fluid which causes this blistering must come up to the epidermis from the vessels of the cutis (exoserosis).

Toxic agents which penetrate the epidermis and reach the cutis result in early vascular dilatation (erythema), edema, nerve injury, induration (cellular infiltration and/or exudation) and sensory distrubances. Of course, such an

agent may cause blistering on its passage through the epidermis, but this will always be delayed in onset whereas sensory disturbances may be early.

The irritation of the epidermis by the agent thus leads to blistering which may later result in the migration of cellular elements from the cutis into the epidermis (exocytosis). The same occurs when bacterial infection supervenes.

The blister may be in the epidermis (intraepidermic vesicle) or under the epidermis (subepidermic vesicle).

Other pathological findings significant for this discussion include:

Hyperkeratosis: Increase in the number of cells of stratum corneum and increase in thickness of this layer.

Parakeratosis: Retention of the nuclei in the cornified cells of the stratum corneum.

Acanthosis: Increase in the numberof cells and size of the stratum mucosum (prickle cell layer). This may be regular or irregular

The appendages of the skin consist of glands (sweat and sebaceous) hair follicles and nails. Theoretically, these structures are important from the point of view of location of lesions, both from vesicant agents as well as the chemicals used to combat them.

The sweat glands areof two types:

1. Apocrine. Large complex glands located in the axillae, anal and genital areas. They secrete an alkaline sweat.

2. Eccrine. Smaller glands which are present over the rest of the body and secrete an acid sweat.

The areas supplied by the apocrine glands are mostviciently attacked by vesicant vapors. Whether thisis fortuitous or due to the pH of the sweat in those areas is at present not known.

The hair and nails consist essentially of keratin, an albuminoid with a high sulphur content. Even though mustard and its derivatives have a marked attraction forkeratin, the hair and nails protect against vesicant gases by:

1. Mechanical barrier, or

2. By absorbing the agent locally thereby preventing deeper effects.

With this sketchy background, it is now possible to discuss the history, pathology, pathogenesis, symptoms, diagnosis, differential diagnosis and treatment of skin injuries due to vesicants.

HISTORICAL

Agents:

World War I.

Chlorine: (Cl)

The first use of gas in World War I was the employment of chlorine by the Germans at Ypres, Belgium, April 22, 1915. This agent has no dermatologic manifestations except caustic effects if the liquid comes in contact with the skin.

Mustard: (H)

On 12 July 1917, the Germans used mustard against the British at Ypres, Belgium. The first large scale use of this agent was by the Germans against the British at Nieuport, France, 21 - 29 July, 1917. There were 14,276 casualties from this agent, 500 of whom died within the first three weeks. This agent was synthesized by the English chemist Guthrie in 1860 and thoroughly investigated by the German chemist Victor Meyer in 1886.

Lewisite: (L)

Was synthesized by Captain Lee Lewis, Chemical Warfare Service, United States Army in 1917. Mixed with mustard it has been used by the Japanese against the Chinese.

Ethyldichlorarsine: (ED).

A vesicant and sternutator, used by the Germans in World War I.

Chloracetophenone: (CN)

A lacrimator which causes skin irritation. It has been reported that the Japs used this agent against the Chinese recently.

Chloracetophenone Solution: (CNS)

Contains chloracetophenone, chloropicrin and chloroform. Is primarily a lacrimator which causes itching of the skin. Not used in World War I.

Chloropicrin: (PS)

Is a lung irritant, secondarily a lacrimator and sternutator. It may cause skin effects if the liquid splashes on the skin. It was first used by the Germans against the Italians on the Western Front in 1917.

Brombenzylcyanide: (BBC)

Was used by the French, British and Americans in World War I.

Sulphur Trioxide-Chlorsulfonic Acid Solution: (FS).

Used as a screening smoke. The liquid causes a caustic burn of the skin. The smoke causes a prickling sensation of the skin. Was not used in World War I.

White Phosphorus: (WP).

Is used as a screening smoke, incendiary and casualty agent. Solid particles of the agent on the skin cause burns. Exposed to air it forms the pentoxide (P_2O_5) if oxygen is plentiful and (P_2O_3), the trioxide, if the oxygen supply is limited. Heat is liberated during this reaction. It was dispersed by means of the 4 inch Stokes Mortar Shell by the British and Americans.

Incendiaries:

Thermite: (TH)

Is a mixture of iron oxide and powdered aluminum. It was used in World War I and the present War as an incendiary.

Combustible Oils:

These are oils mixed with soaps and jellies to form a solid. Particles of metallic sodium are frequently added to rekindle the oil when put out by water, the sodium igniting on contact with water.

Interval Period:

During the interval period between World War I and the present war, innumerable possible new offensive agents were synthesized and studied in the various chemical warfare laboratories throughout the world.

Recent Advances:

The advances made just prior to the onset of World War II and since that time have been mainly concerned with the purification and study of the effects of the well known vesicants. In addition, several derivatives of mustard have been synthesized which promise to have definite vesicant as well as systemic effects. Among these are the so-called Nitrogen Mustards. From the point of view of the vesicant effects, the Nitrogen Mustards are not as effective as mustard. They do however, have special ophthalmological effects as well as systemic effects on the hematopoietic organs. These observations in the main have been limited to animal experiments.

Ointments:

Soon after the introduction of mustard in 1917, frantic efforts were made by the Allies to obtain a protective agent to combat its dermatologic effects. Early in this search ointments were considered to be an ideal method for

neutralization of or preventing the penetration of mustard to the skin.

Among the earliest ointments used were:

Vaseline.
Lanolin
Linseed Oil and various linseed oil derivatives.
Sag Paste (Gas spelled backwards).

Sag Past consisted of boiled linseed oil and zinc oxide or zinc stearate. Data obtained from official American, British and French sources is confused. Some Medical Officers believed these ointments had beneficial effects, others believed the ointments increased the intensity and extent of the burns. In the light of present knowledge both viewpoints might be correct. A definite protective effect is possible in that mustard is soluble in these ointments and its effects on the underlying skin will be delayed. If the ointment is wiped off soon after exposure to slight or moderate amounts of mustard, a burn could conceivably be prevented, whereas, if allowed to remain in contact with the skin, it could conceivably increase the damage.

Toward the end of World War I, the French found that they could increase the protective value of vaseline by dusting bleach powder over the vaseline.

At the close of the war, the status of protective ointments was confused, but the lines of future investigations were indicated in the direction of oxidation by chlorine containing compounds.

In due time a standard United States Army Ointment was developed. After several slight changes in the original ointment, Protective Ointment M4 was made an individual issue. Somewhat later the United States Navy developed a standard ointment (S-461) also based on the oxidizing properties of chlorine.

It can be said that M-4 Ointment presents desireable military characteristics. It is efficient both as a protective and decontaminating agent. It is true that repeated applications will cause dermatitis, but this is evanescent and does not sensitize the individual. In addition to its action against mustard, M-4 Ointment gives creditable protection against lewisite, as well as fairly good (Mechanical?) protection against the new nitrogen mustards.

G-2 reports indicate that the Germans do not have a protective ointment. They do, however, have a chlorine compound in tablet form (Losantin) which is dissolved in water or saliva to make a paste and used to decontaminate mustard. The Japanese and Italians are said to have chlorine containing anti-gas ointments.

BAL Ointments (British Anti-Lewisite):

These are almost specific antagonists of lewisite. The British, the United States Army and the United States Navy each have adopted an ophthalmic ointment containing BAL. These ointments can also be used on the skin to

neutralize and reverse the lewisite effect in tissues. They cannot be used as protectives because of the ease of absorption of the agent and its toxicity.

Hydrogen peroxide in 8% concentration has definite value as an anti-lewisite agent. This is particularly true for liquid lewisite. Solid peroxides have been studied and found of value also. The latter are still being studied.

PROTECTIVE CLOTHING

Protective clothing is of two main types:

1. Impervious.
2. Impregnated.

The former can only be worn for short periods of time, whereas the latter is porous and allows circulation of air. Both woolen and cotton garments can be impregnated.

Protective clothing is very important from the point of view of the dermatologic aspects of chemical warfare. It can be said that the standard clothing as now issued gives efficient protection against mustard and lewisite vapor and efficient initial protection against mustard and lewisite droplets.

During World War I the need for a means of protecting the body against vesicant gases soon became apparent. The most violent burns from mustard occurred in the axillae, groins and on the genitals. The present United States Army protective clothing is efficient.

In regard to protective clothing the problem facing the dermatologist is two-fold:

1. The degree of protection afforded against vesicant gases.

2. The irritation to the skin.

   a. Specific, from the substances used in the impregnating process.
   b. Non-specific from sweat and friction. These are especially important problems in the tropics.

The solvent used in the impregnation of clothing has recently become a strategic material. Furthermore, cases of liver damage, some eventuating in acute yellow atrophy have been observed from the inhalation of the solvent.

IMMUNOLOGIC THERAPY

Sporadic attempts have been made to find a method of combating the effects of vesicant gases on the skin by means of internal agents or alteration of the reactivity of the skin.

Theoretically if strong antisera against mustard can be prepared in animals, these might have curative effects on mustard lesions. Furthermore, mustard

protein combinations could conceivably be used to "immunize" individuals against mustard. Many such studies have been made, but nothing of value has thus far resulted.

METHODS OF DISPERSAL OF THE AGENTS

Detailed technical discussions are not indicated here. A superficial discussion of modern methods is not out of place, however.

The screening smokes and incendiaries which may cause skin effects need no further discussion. Some mention of the methods of dispersal of the vesicants is desirable so that the Medical Officer is aware of essential tactical factors.

In World War I, the burns from mustard were due to vapor and liquid. In modern warfare one can expect to find extensive liquid burns.

Depending on what is desired, the following methods of dispersal may be used:

1. Mortar shells.

2. Artillery shell.

   a. Air burst.
   b. Ground burst.

3. Land mines.

4. Airplane spray.

   a. High altitude.
   b. Low altitude.

5. Airplane bombs.

   a. Air burst
   b. Ground burst
   c. Delayed action

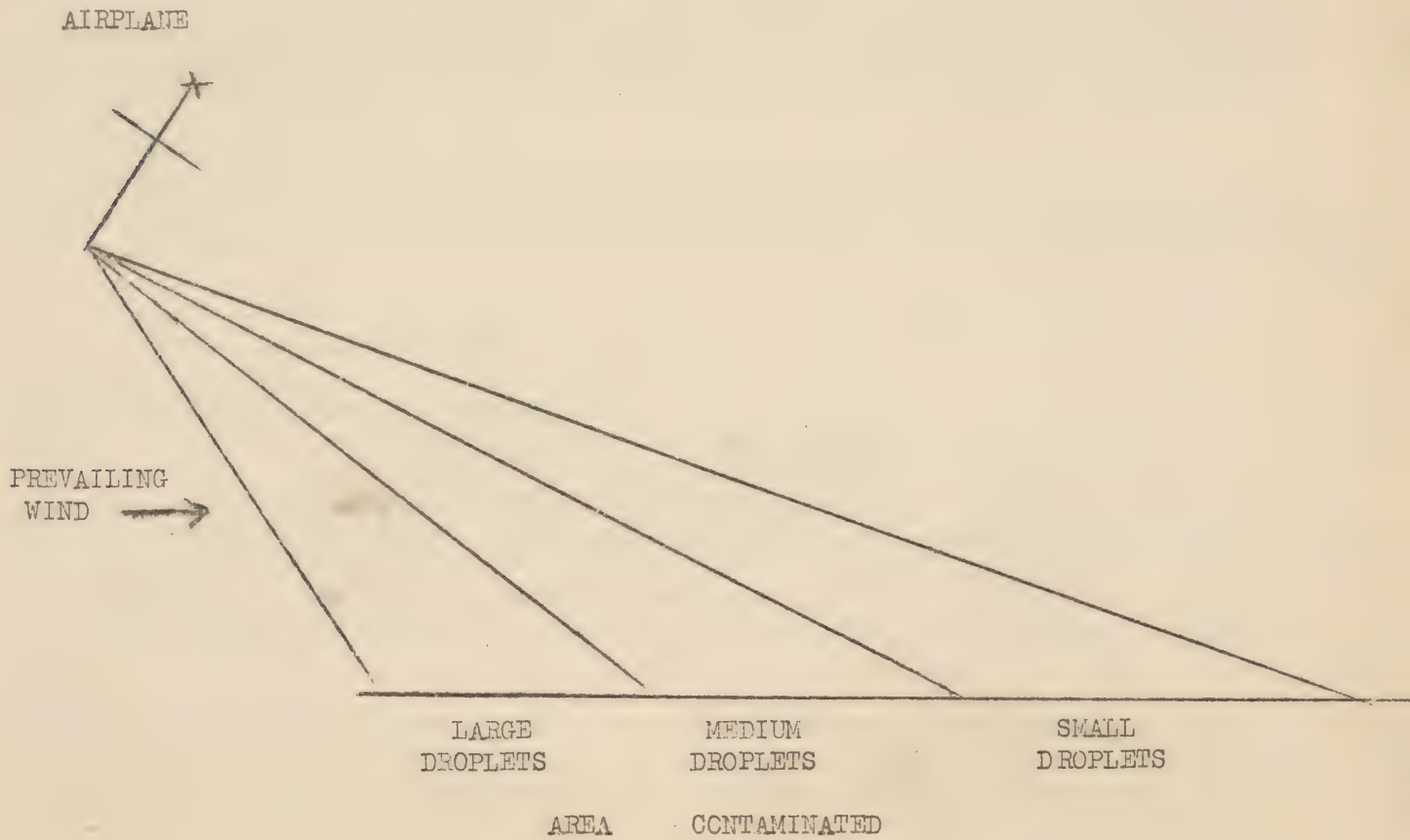
6. Grenades.

It will suffice to state here that if and when vesicant gases are used they will, no doubt, be used in amounts undreamed of in World War I. Consequently personnel must be well trained in defence against vesicant attack and in personal decontamination after such attack. If this training is not efficient we must be prepared to accept large numbers of casualties.

The airplane spray method of disseminating vesicant agents has many special features. Among these are:

1. Surprise low altitude attack which will disseminate droplets of vesicant.

2. High altitude attack. By this method planes flying at high altitudes release liquid vesicant which is transformed into droplets by the slip stream. On their travel to the ground there will be a definite loss in volume of the individual droplet due to evaporation. Here, many factors will influence the quantity of vesicant which will strike personnel. Recently "thickening agents" have been used and the size of the droplet can be controlled by means of these added materials. It must, however, be pointed out that the enemy can frequently change the conditions at will with which he sprays personnel, either by increasing or decreasing his elevation or altering his course in relation to the prevailing wind. It can be said that high altitude spray attacks will result in general contamination of personnel by droplets and frequently by an unseen, unheard plane, which usually will be many miles lateral to the area attacked. This can best be demonstrated by a diagram:



The effects will be more or less general and will resemble those of vapor rather than liquid except when "thickened" vesicants are used. If the latter are used large drops can form. The other methods of dispersal mentioned above are self-explanatory.

RECENT ADVANCES AND PREDICTIONS

Recent advances in agents and protectives should be briefly mentioned. It is possible that the enemy will use a different type of mustard than he used

in World War I. Modern chemical research has yielded methods for producing a pure grade of mustard and lewisite. Purified or initially pure mustard has many military characteristics which should be mentioned:

1. It is practically colorless.
2. It has much less of the characteristic odor of impure mustard.
3. It does not attack metals readily and consequently will not deteriorate on storage.
4. Smaller quantities will give maximum effects.

Several predictions are warranted from our present accumulated knowledge:

1. Mustard is still the best all round vesicant agent. It is persistant, easily handled, has a high vapor pressure and causes local and systemic effects. Furthermore, no specific or even highly effective antidote has been found. Furthermore, its effects are insidious in onset and painless early, which usually excludes early decontamination procedures if the individual is not aware of contamination.

2. Lewisite has never had a real "battle trial". It is still somewhat of an unevaluated enigma. Lewisite hydrolizes readily on contact with water. Consequently it is not likely to be used on raining, foggy or wet days. It will not be used on wet terrain. If so, it will not be an effective casualty producer. Lewisite vapor is probably a negligible factor under field conditions regardless of the weather. Casualties from lewisite will mainly be from liquid contamination. It is, furthermore, comforting to know that two effective anti-lewisite agents are available for first aid, namely:

a. Hydrogen peroxide
b. BAL

3. Mixtures: There is little doubt in the minds of many people that when and if the enemy uses vesicant agents, mixtures of mustard and lewisite will be employed. The problem of first aid and decontamination becomes complex. The definitive treatment, however, is the same.

4. Nitrogen Mustards: While these are much less effective vesicants than is mustard, they are important and it is known from G2 sources that the enemy has these agents on hand. Though the vesicant effects of nitrogen mustards are not as great as mustard, they do apparently possess the power to penetrate the intact skin and cause systemic toxic (haematopoietic organs) effects. The lack of strong odor and the absence of any other identifying characteristic increases their importance.

PATHOLOGY

PATHOGENESIS OF VESICANT EFFECTS:

Mustard: As is well known mustard is an oily liquid at ordinary temperatures. It is soluble in most fat and fat solvents. This is very important in understanding the localization of burns and local intensities of effect. Furthermore,

mustard vapor seems to have a predelection to effect areas supplied by the apocrine sweat glands (axillae, genital area). Whether this is dependent on the type of sweat secreted here (alkaline) or due to other factors is not yet clear. It is also wise to remember that where liquid mustard is concerned there will also usually be concomitant vapor effects. The converse is not necessarily true.

Mustard seemsto possess a special predelection for dermatologic structures, particularly the epidermis and its derivatives. This effect may be due to the presence of keratin in these structures. Extensive studies of mustard-keratin relationships has not yet yielded a method of combating this reaction or reversing the combination once it has occured.. Valuable information as to the mechanism of the union,has, however, resulted from these studies.

There is little doubt that the maximum toxic effect is on the epidermis and that subepidermic effects also occur. This is borne out by observed clinical and pathological effects. The presence of a thick keratin layer frequently protects deeper structures. It seems likely that because of the attraction of mustard to keratin such thick layersof keratin probably absorb and hold or neutralize the mustard, thereby protecting deeper structures. Thus mustard burns of the palms of the hands, soles of the feet, scalp (protected by hair) and under the nails are rare.

It is said that even if the respiratory and gastro-intestinal tract are efficiently protected by the gas mask, systemic effects are obtainable by means of massive absorption through intact skin. These effects are said to consist mainly of gastro-intestinal injury with hemorrhage as well as liver damage.

Ingested mustard causes gastro-intestinal hemorrhage, necrosis, intense pain, and some bone marrow effects consisting in great part of leucopenia and agranulocytosis.

Inhaled mustard vapor may cause effects on the whole respiratory tract involving especially the trachea and larger bronchi. The alveoli are more or less spared. These effects consist of rhinitis, pain in the nose, sneezing, edema and necrosis of the vocal cords, cough, retrosternal pain, ulceration and necrosisof bronchial mucous membranes leading to sloughing which in turns results in coughing up bronchial casts, sepsis, lung abscess, broncho-pneumonia.

Mustard vapor and liquid causes severe edema of the eyelids and conjunctivae with keratitis and ulceration of the cornea.

MECHANISM OF ACTION

Here we are exclusively concerned with dermatologic effects. During World War I and afer, the accepted theory of mustard action was the one evolved by Marshall. This assumed that when mustard came in contact with animal tissues it hydrolized to yield hydrochloric acid which in turn caused the local injury. This theory has been disproven by recent studies of dissociation constants,

products of hydrolysis, local effects and by a study of the effects of radio-active mustard on tissues (the latter prepared from radio sulphur obtained in cyclothron). It is now fairly well established that the specific effects of mustard on tissues is due to the whole mustard molecule. Just how this acts and exactly where the protein molecule is attacked is at present not yet definitely known. Whether the addition of the mustard into the protein molecule is by displacement of Cl (the most likely theory) or by the displacement of an H (which is unlikely) or at the S linkage (a possibility), is not yet completely settled. Much information is accumulating each day which may completely clarify the situation in the near future.

Effect on Enzymes: All this research into the mechanism of mustard action has resulted in the definite fact, namely, that mustard inhibits certain of the tissue enzymes and enzyme systems. Whether all the effects due to mustard can be attributed to this effect alone has not yet been decided. The probability is that other factors also enter into the picture.

A report from Edgewood Arsenal claims that mustard has no effect on striated muscle, accounting for the rarity of deep effects. A recent National Defense Research Council report, on the other hand, states that mustard does cause reactions in striated muscle tissue. The local effects on nerve and intestinal tissues have also been studied.

In conclusion it may be stated that mustard:

1. Is soluble in fat and fat solvents.
2. Has an attraction for keratin.
3. Exerts its main effects on epidermis and epidermal derivatives.
4. Causes less obvious effects on subepidermal structures.
5. May be absorbed locally to cause internal effects.
6. Causes definite ophthalmologic, respiratory, and gastro-intestinal effects when these organs are directly exposed.
7. Its effects on tissues are due to the whole molecule.
8. The mechanism of its action is not yet completely known.
9. It has definite inhibiting effects on certain enzymes and enzyme systems which may in part, at least, explain some of its effects.

Lewisite: The mechanism of lewisite action has not been as intensively studied as has that of mustard. However, lewisite, too, probably also acts as the lewisite molecule since its derivatives are relatively non-vesicant, although the products of hydrolysis still have violent systemic toxic effects. Lewisite is also soluble in fat and fat solvents and that which was said for mustard in this regard, also holds true for lewisite. Lewisite differs from mustard in one regard, however, in that it causes early pain and erythema when applied to intact skin. This would suggest that the agent penetrates the epidermis more easily than mustard and exerts early cutis effects. Furthermore the marked attraction to keratin is not so apparent with lewisite. Histologic examination of lewisite burns in various stages of developments bears out these facts, i.e.

early penetration of the epidermis and early cutis effects. Absorbed lewisite may cause systemic effects which are mainly those of the tri-valent arsenic (liver and kidney damage). Lewisite, too, will cause respiratory, ophthalmologic and gastro-intestinal effects when the vapor or liquid comes in direct contact with these organs.

Nitrogen Mustards: The nitrogen mustards thus far studied while less vesicant than mustard itself apparently exert their vesicant effects in the same manner as mustard. This group of agents also (in animals at least), can be absorbed from the skin and cause injury to the hematopoietic system and when the vapor is inhaled in humans cause severe pulmonary involvement.

Mustard-Lewisite Mixtures. The mechanisms here are those of each agent, and have an added advantage in that the freezing point is lower than that of each of the individual components.

PATHOLOGY

Mustard: When applied to human skin mustard causes no immediate effects. Changes appear in 4 to 24 hours, depending on climate, concentration, length of exposure and individual susceptibility. These consist first of erythema, later edema and finally vesiculation, which becomes progressive with large doses. The blistering effect reaches its maximum in most individuals in 48 hours. The blister first contains clear serum, which later may become turbid and in 48 to 72 hours has steep sloping sides. Later, the blister if unruptured becomes flaccid and if no infection has occurred, the fluid is gradually absorbed. Usually, however, the blister ruptures spontaneously during this period. There is always a halo of erythema around the blister and after 48 hours infiltration may occur, but it is difficult to distinguish this from the edema present in the lesion. Infiltration is usually not an outstanding characteristic. If for any reason the top of the blister is rubbed off, usually an erythematous, glistening, bright red "raw beef" base is noted. Occasionally the base (especially in severe burns) may present a grayish "cooked appearance", and with very severe lesions the base may be necrotic. The blister fluid is not vesicant although the material of the blister base is irritating. As the lesion heals it is usually replaced by a thin layer of new skin. Scarring is uncommon in uncomplicated cases, although brownish red pigmentation frequently occurs in the area and may persist for months.

It is not uncommon after 24 hours to see an annular arrangement of the vesicles which later coalesce to form a uniform lesion.

When large droplets of liquid mustard come in contact with human skin it is not unusual to find an annular blister surrounding a central anemic zone. In such cases the blister never encroaches on the central zone. The central area takes on a "cooked" appearance and eventually becomes necrotic. The central necrotic area frequently sloughs off leaving an ulcer. Depending on how deep the destructive lesion has gone, scarring occurs after healing. The resultant scar is usually thin and pliable.

If exposure to the agent was only for a short time or if the concentration of the agent was minimal, erythema only occurs.

Microscopic Findings:

Early biopsy of the mustard lesion reveals nothing. Varying with the individual, but usually quite apparent after 8 to 12 hours, evidences of epidermal injury are demonstrable. In the usual case which will eventuate in the formation of a uniform blister, intercellular epidermal edema is observed (spongiosis, microscopic vesiculation). The cells of the epidermis are attacked (especially those of the basal layer) and the cells disintegrate and apparently liquify. Later, intercellular bridges are ruptured, adjacent injured liquified cells coalesce and fusion of the microscopic vesicles results in larger accumulations of fluid (clinical vesical). As this process progresses and fusion of adjacent vesicles occurs bullae result. This blistering with mustard is always intra-epidermal. Although changes occur in the cutis (vascular dilatation, edema in and between the connective tissue fibers) the results are not very striking. Perivascular accumulation of cells is not prominent (as a matter of fact noteworthy by its absence). Thus the main pathological effects of mustard occur in the epidermis.

The fact that the basal layer is the active proliferative area of the epidermi and since the cells of the basal layer are apparently preferentially attacked suggests that the active metabolism of these cells somehow enters into the picture. Whether or not mustard acts here by its well known effects on enzymes is a possibility but is as yet only an attractive unproven hypothesis.

These pathological effects can at this point be correlated with the preceding discussions of the anatomy and physiology of the skin, and with the known facts of the pathogenesis of mustard skin lesions and with clinical symptoms if the latter are anticipated at this point. Thus, mustard possesses an avid attraction for epidermal structures. It exerts its main effects on the epidermis. Consequently, few cutis effects occur. Since the epidermis contains no nerves or blood vessels, pain, itching, erythema and edema are delayed. Since the only available early epidermal responses are edema or necrosis depending on the intensity of the stimulus, one or both of these may occur. If the toxic effect is average, edema is the main form of response. Since there are no blood vessels in the epidermis, fluid must seep up from the vessels of the cutis (exoserosis). This is a slow process. That is why it may take 48 to 72 hours for blistering to occur.

The fact that observable microscopic epidermal pathological reactions are delayed in onset does not necessarily give promise that eventually a means of reversing the mustard tissue injury will be found. The long lag period has been said to give such hope i.e. there is so much time between contact and appearance of reaction. This attractive hypothesis can be refuted by the known sluggishness of epidermal reactions. The injury has been done but the effects are not immediately observable.

Apparently the great attraction for epidermal structures which mustard possesses, appreciably slows its passage to the cutis. Mustard or products derived from its disintegration may eventually reach the cutis. It may be that in the average type of stimulus mustard or its products of disintegration never

reach the cutis. The responses here in such cases could be due to the demands made by the overlying injured epidermis. Regardless of how cutis stimulation eventually occurs, the final outcome is itching, pain, edema and erythema.

Microscopically, the annular type of vesicle with a central necrotic zone shows the above phenomena in the vesicular portion while the central area reveals coagulation necrosis.

When the vesicular lesion of a mustard burn heals, the previously involved area shows loss of papillary bodies and rete pegs and hyperkeratosis.

It can be concluded that:

1. Mustard primarily causes epidermal injury.

2. The average effect is vesiculation due to edema of the epidermis.

3. These effects are delayed in onset because of the notorious slow reactions of the epidermis (mainly due to the absence of blood vessels).

4. The mustard blister is intraepidermal.

5. Coagulation necrosis of the epidermal cells may occur with large doses.

6. Cutis effects are late and minimal in degree, consisting mainly of edema and vascular dilatation.

Lewisite:

This agent when applied to human skin as a vapor or liquid causes early subjective clinical signs (pain, burning etc). The objective signs are rapid in onset (15 minutes to 4 hours) with early appearance of erythema and edema. Vesiculation again parallels the phenomena described for mustard, namely, delayed onset. In other words as stated previously, epidermal reactions are slow in onset and slow in developing. The types of blistering roughly parallels those described for mustard. The isolated lewisite blister differs from the mustard blister in that it has bulging sides, (ping-pong ball blister). The blister usually rises from practically normal skin, i.e. little erythema. Careful inspection, however, will usually reveal a small halo of erythema, but certainly not as extensive as that observed in mustard burns. The lewisite blister has less tendency to rupture spontaneously. The blister is subepidermal. Therefore, a larger layer of tissue forms the covering of the blister. This may explain the greater resistance of the blisters. The area burned by lewisite differs from the mustard area in that definite infiltration is usually apparent. As the blister heals the same train of events as described for mustard occur. Pigmentation is, however, uncommon.

With lewisite, the epidermal reactions described for mustard also occur to a degree. All lewisite effects seem to occur at deeper levels. Marked early

changes are noted in the cutis which shows edema, vascular dilatation and cellular reaction, the latter being in part perivascular.

Thus, in attempting to correlate anatomical, physiological and pathological phenomena with clinical effects one can state that lewisite, too, is attracted to epidermal structures but in addition is markedly attracted to deeper structures. One of the possibilities to consider is that lewisite is primarily attracted to subepidermal structures (blood vessels, nerves, connective tissue) and merely exerts its toxic effects on the epidermis during its passage down to deeper structures, more or less as a secondary side effect. This, then, would explain why lewisite causes early pain, early erythema, early edema and later induration (cellular response). Here again nothing (not even highly toxic lewisite) can make the sluggish epidermis speed up its reaction. Thus, the lewisite blister, too, is late in appearing even though it does usually appear somewhat earlier than the mustard blister.

To summarize:

1. Lewisite causes epidermal and marked cutis injury, (Possibly the latter is its primary toxic effect, while the former may be an accidental effect due to the interposition of the epidermis between the outer world and lewisite's site of predelection of action).

2. Vesiculation occurs as an average effect.

3. The blistering effects are delayed in onset because of the sluggish reactions of the epidermis.

4. The blister is subepidermal.

5. Coagulation necrosis may occur with large doses.

6. Cutis effects are early, consisting of edoma, vascular dilatation and cellular exudation. (It appears that lewisite soaks into the tissues so that it can exert its systemic toxic effects).

Nitrogen Mustards:

Significant amounts of human biopsy or necropsy material is not available at this time. Deliberate experimental application of these agents to the human skin has demonstrated that this group is vesicant, but much less so than mustard. It has been assumed that the pathogenesis is the same as for mustard. Accidental inhalation by workers in factories manufacturing this group of agents reveals symptoms similar to those resulting when mustard is inhaled. Blood studies in these patients have not confirmed the results of animal studies in which marked leucopenia and agranulocytosis were found. In addition these animal studies revealed skin irritation and marked gastro-intestinal symptoms resulting from skin absorption of the agents. Animal inhalation and ingestion experiments give results similar to those observed with mustard.

Incendiaries and White Phosphorus:

These cause their effects mainly by heat and are therefore thermal burns. In the case of white phosphorus in addition to the heat there is also an associated chemical factor, due to the formation of phosphorus pentoxide or trioxide.

SYMPTOMS

Although objective symptoms have been more or less discussed above, it would be well to summarize them at this point. Whether sexual, or racial susceptibility or immunity to vesicants exists is problematical. Physicians who have observed numbers of vesicant burns in industry in general feel that females are more susceptible than males and that negroes are more resistant than whites.

Mustard: It is probable that no one is immune to the skin effects of mustard. Some individuals may, however, be more sensitive than others, even if they have not come in contact with the agent previously.

Mustard Vapor: When mustard vapor in minimal concentrations comes in contact with unprotected human skin, erythema and some edema occur in the exposed sites. Usually no signs occur for 4 to 12 hours. At that time a faint blush is noted in the area accompanied by subjective symptoms of itching. The latter symptom becomes progressively worse and in most individuals becomes intractible and intense. It is characteristic that the usual antipruritic armamentarium of the dermatologist isof little avail here. In 24 hours the erythema is manifest and the itching frequently ceases although the sensation of local heat may continue. The erythematous area after 24 to 48 hours becomes slightly edematous but never markedly so. Depending on individual susceptibility and the quantity and length of exposure to the vapor, the erythema subsides gradually. This usually occurs anywhere from 4 days to a week. Thereafter the area previously involved by erythema may show various degrees of pigmentation in different individuals. The pigmentation varies from a slight tan to a deep mahogany brown. In negroes the burned area may be ebony black, even in mulattoes. If the vapor exposure was slight, complete restitution occurs. If more intense, slight to moderate scaling may follow. The area usually heals completely with no observable evidence of previous injury, other than pigmentation. The site may, however, be more sensitive than normal to thermal, mechanical and chemical insult for some time. If the vapor concentration or exposure is greater, symptoms supervene which are comparable to those which occur when liquid mustard is splashed on the skin.

Liquid Mustard: When liquid mustard comes in contact with human skin a characteristic train of symptoms occur. The liquid rapidly disappears from the skin surface and literally seems to be sucked into the skin. Here again no signs and symptoms are apparent for hours. After 4 to 12 hours erythema and slight edema are noted. Preceding this by an hour or two slight stinging, itching and burning may be apparent. With the onset of erythema, itching becomes intense. (here there is great individual variation). Beginning anywhere from 12 to 24 hours vesiculation becomes apparent. In some cases it is delayed as long as 48 hours. This vesiculation is at its height in most cases between 48 and 72 hours.

(See section on Pathology for details). When vesiculation becomes fully manifest, the subjective symptoms usually cease. When secondary infection does not occur the area is usually healed in 14 to 18 hours.

Lewisite:

Vapor: It is unlikely that lewisite vapor as such alone will be of great importance because:

1. The vapor pressure is lower than mustard.

2. The vapor hydrolyzes easily on contact with water (or water vapor) to yield non-vesicant compounds.

3. The odor is characteristically pungent and irritating to the nasal mucous membranes and gives adequate warning.

4. Soon after contact with the skin, pain and itching are a warning sign.

If, however, the vapor of lewisite is present in adequate concentration, burn may occur. Here, too, as with mustard erythema, the symptoms are somewhat delayed in appearance, yet they regularly occur earlier than with mustard. (The possible theoretical reasons for this have been discussed). The erythema in mild exposures appears in 15 minutes to 4 hours. Pain, stinging and burning is an early accompaniment of lewisite burns. Here again the clinical course resembles that of mustard with one exception and that is that pigmentation is uncommon.

Here, too, when the vapor concentration is high or the exposure time long, symptoms supervene which are comparible to those which occur when liquid lewisite is splashed on the skin.

Liquid Lewisite: The symptoms here again resemble those described for mustard (but with the differences noted in the section devoted to Pathology above). In several respects the train of symptoms in liquid lewisite burns differ from those of mustard. These are:

1. Early onset of subjective signs, e.g. burning, stinging, pain. These occur shortly after lewisite touches the skin.

2. Earlier onset of erythema and edema.

3. Presence of definite induration.

Neither mustard or lewisite blister fluid is vesicant when it comes in contact with uninvolved areas.

Nitrogen Mustards: Here the symptoms are the same as those of mustard except that they are less intense with comparable exposures.

Incendiaries and White Phosphorus: With incendiaries the train of symptoms

are those of thermal burns. The symptoms from contact with solid white phosphorus particles are those of the thermal burn plus the added chemical burn due to the formation of phosphorus pentoxide. These burns are deep and torpid as are most chemical burns.

COMPLICATIONS

Mustard: The main local skin complication of mustard burns is secondary infection. Early in World War I this was difficult to combat. When the Carel-Dakin Method of treatment was instituted in these cases the incidence of severe effects from the secondary infection became much less. Recently with the improvement of surgical technic and the introduction of the sulfonamides in therapy infection in such burns is rare indeed.

The systemic effects of mustard locally applied (assuming efficient protection of the respiratory and gastro-intestinal tract by a gas mask) are said to be mainly edema and hemorrhages of the gastro-intestinal tract and liver damage, (edema, necrosis). During World War I the almost uniform absence of systemic complications even with extensive skin injury was striking. Vomiting was occasionally noted soon after the burn, but direct effects on the gastro-intestinal tract in these cases by swallowed mustard (vapor or liquid) could not be ruled out.

Lewisite: Since a large series of cases is not available, a complete evaluation at this time is impossible. With lewisite one finds the same local complications as with mustard. Lewisite locally applied in sufficient quantity will, very likely, cause marked systemic complications. The usual systemic complications from toxic concentrations of tri-valent arsenic can occur. Among these are:

1. Gastro-intestinal edema and hemorrhages.
2. Edema, fatty degeneration and necrosis of the liver (toxic hepatitis, acute yellow atrophy).
3. Exfoliating dermatitis.
4. Various types of "drug eruptions".
5. Nephritis.
6. Encephalitis (edema, hemorrhages).
7. Leucopenia, agranulocytosis.

Non-infected lewisite and mustard burns usually heal in about the same time as a comparable thermal burn.

Nitrogen Mustards: Here the local complications will probably be the same as for mustard. In addition marked systemic effects are said to occur from local skin absorption (animal experiments). These are mainly:

1. Involvement of the hematopoietic organs with particular suppression of the granulocytes. The agranulocytosis so produced does not respond to pentnucleotide therapy.

2. Gastro-intestinal and liver symptoms resembling those occuring with toxic absorption of mustard.

Incendiaries and White Phosphorus: The complications are those of thermal burns in general.

SEQUELLAE

Here need be mentioned psychological factors occuring in personnel previously burned by the vesicants, and sensitization (local and general) which occurs after contact with mustard and possibly with mustard derivatives as well. It is characteristic that an individual whose skin has been previously burned by mustard, is thereafter more sensitive to this agent. This increased sensitivity is more or less universal in individuals previously burned. Such a person reacts more violently to smaller doses of mustard. Certain individuals who have been burned several times with mustard become so exquisitely sensitive that minute concentrations of vapor may call forth maximum responses. Not only may there be erythema and blistering, but even urticarial lesions may occur. The other cases in whom only a small area was burned may not show generalized sensitivity but may present a striking localized sensitivity of the burned area. This area may be sensitive not only to mustard, but to other thermal, physical, and chemical insults.

The following is an interesting observation made in the mustard manufacturing plants at Edgewood Arsenal. Individuals are known who have been exposed to mustard vapor for years, (all personnel wear impregnated clothing), without apparent ill effects, i.e., no generalized sensitivity. When, however, such an individual's skin is splashed with mustard and blistering results, that individual will frequently become violently sensitive even to minimal concentrations of mustard vapor. Thereafter he is unable to withstand even such mild vapor exposures as are present in the plant and may react with conjunctivitis, keratitis, erythema of the skin, blistering, respiratory tract irritation, pulmonary edema, edeam of the glottis and even general symptoms of profound intoxication. The dermatotropic proclivities of mustard are again demonstrated here and the alterati of the individual by such contact is apparent.

Lewisite: Even though a few isolated cases of increased sensitivity to lewisite on repeated application have been reported, in general it can be said that lewisite does not cause increased sensitivity on repeated application.

Scarring: Severe, deep, ulcerating, or infected mustard or lewisite burns may cause scarring.

Incendiaries and White Phosphorus: These, of course, may cause scarring if the injury extends into the cutis (where replacement of injured tissue can only be by fibrous connective tissue). Unfortunately, the injury frequently does extend into the cutis.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of the agent used is important immediately after injury in order that specific first aid measures can be taken. The sooner after contact with the agent that specific measures are taken, the less liklihood there is that a severe burn will occur. Thus, it must be stressed that personal decontamination is the responsibility of the individual. In the case of liquid mustard or lewisite on the skin or in the eye, this must be done within the first five minutes, even earlier in a hot humid climate. Recent experiments in Queensland by the Royal Australian Medical Corps revealed that in tropical, humid climates vesicants cause excessively severe burns and protective clothing and existing ointments have little protective value. The irreversible union of vesicant to tissue also seems to be accelerated. The responsibility for the detection of the agent in the field, therefore, is a unit and individual responsibility. If personal decontamination is delayed or troops are inadequately trained, severe effects can be expected.

Once the symptoms are manifest and with inpouring Intelligence and Chemical Warfare Service reports there should be no difficulty in recognizing the cause of later vesicant burns. Furthermore the fact that many individuals are affected by similar lesions makes the diagnosis relatively easy.

Differential Diagnosis: This isof importance particularly under noncombat conditions. Thus, a group of men might be marched through underbrush in an area where chemical agents were used previously. Several of the individuals may present themselves in 24 to 48 hours with an erythematous, edematous and vesicular eruption. In such cases and in the factories in which Chemical Warfare agents are handled one must consider:

Contact (Plant) Dermatitis: In this Theater of Operations, reports have come in that blisters similar to those caused by mustard have been produced by contact with Wild Parsnip plants. Cases are reported that occurred 48 hours after contact with the plant. No other organs, except the skin, are involved by contact with this plant. Even contact with edible parsnip is said to occasionally cause the same symptoms. In this theater it would be wise for medical officers to investigate the presence of Wild Parsnips in the area where they are stationed, particularly if blistering skin eruptions are noted in troops.

Any plant can cause the above type of reaction. It is characteristic of plant dermatitis that the symptoms i.e. vesiculation, occur about 48 hours after contact with the plant and that only the skin is involved, the mucous membranes of the eyes and respiratory tract being spared. The latter is not ture of burns due to the classical vesicant agents. It is said that in most cases of plant dermatitis, the resins and oils of the plant are responsible for the symptoms.

A typical plant dermatitis will usually somewhere show vesicles in a linear arrangement.

Other substances including dyes, local anaesthetics, metals (and their salts), detergents, solvents, industrial chemicals, cosmetics, clothing, etc., may cause a blistering dermatitis in individuals who have previously come in contact with these substances (or derivatives of these substances). Also in predisposed individuals (even though previous contact has not occurred), sensitivity may develop rapidly and characteristically is ushered in by the "flare-up" reaction which usually occurs 6 to 14 days after the original contact. This reaction is usually sudden in onset and severe in degree with erythema, edema and blistering. Thereafter, the whole skin is sensitized to the material and will present in 12 t 48 hours after contact, a blistering dermatitis.

A careful history of the present eruption and events which preceded it, a careful past history of previous similar episodes and proper application and evaluation of patch tests will be of value. Proper values for concentrations of materials to be applied in these tests can be obtained by consulting such texts as Sulzberger's "Dermatologic Allergy". Previous experience is vital to proper application and evaluation of such tests. Most dermatologists have had this experience.

Irritant Dermatitis: Acids, alkalies, detergents and solvents are usually responsible here and the lesions usually occur on the hands and arms.

Burns from other agents: Chemical, physical and thermal burns must be considered. The history will usually make the diagnosis.

Other Dermatoses: These need only be listed since they are rarely important:

1. Primary vesicular fungus infections and vesicular dermatophytids.
2. Beginning Impetigo Contageosa.
3. Bullous erythema multiforme and multiform erythema.
4. Erythematous and bullous drug eruptions.
5. Pemphigus.
6. Epidermolysis bullosum.
7. Choiropompholyx (dysidrosis).
8. Pustular psoriasis.
9. Recalcitrant eruption of Andrews.
10. Bacterids, monilids, etc.

11. Variola, varicella, herpes zoster, herpes simplex.

12. Vesicular syphilis (rare in whites, occurs occasionally in negroes).

PROGNOSIS

Reasssurance of the patient is extremely important. Vesicant gas casualties rarely die and rarely have permanent defects. It is true that deep infected burns and the anemic, necrotic type of burn may ulcerate and cause scarring. This, however, fortunately is not frequent. Iternal complications will usually clear up under proper treatment without sequellae. Thus, in practically all cases the prognosis can be summed up in one word - excellent. Massive extensive, untreated burns can, however, be fatal. First aid measures must be efficiently and immediately applied.

TREATMENT

Treatment of vesicant skin injuries is a special complex problem. In the early management of such cases, ordinary dermatologic management directed to the morphology of the lesions is not adequate. Treatment falls into three completely separate categories:

1. Prophylaxis (Protective Measures).
2. First Aid.
3. Definitive Treatment.

Prophylactic (Protective) Treatment. This is covered in this theater of operations by Training Memorandum 42, Hq ETOUSA, 23 December 1943, and lists the following individual issue of protective equipment:

1. Gas Mask.
2. 1 Tube of Protective Ointment.
3. 4 Eyeshields (2 to be held in unit storage).
4. 2 Protective Covers (1 to be held in unit storage).
5. 2 Sleeve Detectors.
6. 1 8 Oz. Container Shoe Impregnite.
7. 1 Complete suit of Impregnated Clothing (to be held in storage).
8. Eye Ointment BAL, MD Item 1K24808.

Nothing further need be said about the above. When it is known that vesicants have or are about to be used the well trained soldier will take protective measures by use of the above equipment.

First Aid Treatment. In a letter from the Adjutant General to the Surgeon General dated August 1942, First Aid was defined as: "First Aid consists of those measures which the individual soldier can perform for himself or his comrade with the means available to him in the field". First aid to himself by himself is

the responsibility of each individual exposed to gas attack. Speed of action is essential and can be had only by such individual action.

Since the vesicants are so rapid in their union with tissues and since this union becomes irreversible in a matter of minutes, it can be seen that immediate personal decontamination is the responsibility of each individual and only by this means can large numbers of vesicant casualties be avoided. Therefore, efficient gas discipline and training for all troops is an absolute necessity. Chemical attack should have little effect on an efficiently trained army. In such cases it can only act as a "nuisance factor". Furthermore, the psychological effects of such training are of great value to morale, since if chemicals are used, a military unit if well trained will not be disorganized, but will be able to carry out its mission with little or no delay.

In this Theater of Operations First Aid against vesicants is also covered in Training Memorandum 42, mentioned above. The following is an extract of this directive applying to skin injuries:

Supplies for First Aid available to Soldier in Field:

1. Protective Ointment, CWS issue; carried in gas mask container.
2. Soap, toilet or issue; carried in pack.
3. Water, canteen.
4. Gasoline (motor fuel); fuel tanks of motor cars or airplanes.
5. Cloths or rags, handkerchiefs or parts of clothing.
6. Kit, first aid, gas casualty; carried on combat vehicles and tanks; directions in kit.
7. Eye Ointment BAL, Medical Department issue, Item 1K24808.

First Aid against vesicants (Mustard gas, Lewisite). If the face is contaminated with liquid vesicant, the mask must not be put on until the face has been decontaminated by means given below:

1. Skin. When drops of suspicious or "smelly" liquid are sprayed or splashed on skin:

   a. If protective ointment is available. Blot off liquid with absorbant paper, cloth, rag or vegitation. Apply liberal amount of protective ointment M4 (or M1) and rub in well with fingers. Rub off with paper or cloth. Repeat 3 times; then burn or bury these cloths or papers. If clothing is contaminated remove at first opportunity. Bathe as soon as possible.
   (CAUTION: Do NOT put ointment on skin if it is red or blistered).

   b. If protective ointment is not available; Moisten (not wet) cloth or rag with motor gasoline. Dab or blot contaminated areas with this cloth. Do not rub with cloth or your spread the gas. Repeat 6 to 10 times, using freshly moistened cloths. Wash areas with soap and water, better if hot, at first opportunity. Burn or bury these cloths

c. If neither ointment or gasoline is available: Work up heavy lather on damp cloth, using water (canteen) and soap (pack). Dab lather well on contaminated areas but not on clean skin. Wipe lather off. Repeat several times.

If a vesicant is encountered in vapor form, first aid will be of little value. In such cases prophylactic measures are of most importance. The exception is BAL Ointment of Solution in the case of lewisite vapor burns. This will be of benefit.

Assuming that an individual has been sprayed with a liquid vesicant, the first procedure will be to follow the above recorded directive. In any case if the eyes are contaminated they will be treated first and then the above procedures will be carried out on the skin. If the clothing is badly contaminated it must be removed. The upper clothing near the face and neck must be immediately removed or at least removed before other clothing is removed. If only a few splashes of vesicant are present, they may be cut away. If Protective Clothing is worn and it, too, is badly contaminated it must be doffed.

After decontamination, the soldier will resume his mission. If efficiently trained in this procedure, a few vesicant casualties should occur. If the situation is such that time is not available to even perform personal decontamination completely, the commanding officer of a unit may decide to continue the mission and accept the resultant casualties. If the situation demands he can do this since the effects of the vesicants are delayed in onset. Later the casualties may be treated and those with lesser injuries may carry on even though blisters are present. (See Suffield Report below). Manifest vesicant casualties will report to the Medical Department for treatment.

Treatment will vary in the different echelons of the Medical Service. If an individual has been exposed to a vesicant and if for some reason has not been able to perform effective personal decontamination, he reports to forward echelons for decontamination, i.e. ointment, hydrogen peroxide etc. Such aid stations will possess a Gas Casualty Chest (or its equivalent). The Chest contains (among others) the following supplies for the treatment of vesicant casualties:

1. M-4 Ointment.
2. 16 2/3% Dichloramine T in triacetin.
3. 8% Solution of Hydrogen Peroxide.
4. 5% BAL Solution.
5. Pontocaine Ointment.
6. 5% Sulfadiazine Ointment.

The same supplies are available in all rear echelons including Fixed Medical Installations. One Gas Casualty Chest (or its equivalent) is supplied per 250 bed capacity. In addition all combat vehicles (armoured cars, tanks, half-tracks etc) contain Kit, First Aid, Gas Casualty. This item contains for the handling of vesicant casualties:

1. M-4 Ointment.
2. BAL Solution
3. Pontocaine Ointment.

4. 16 2/3% Dichloramine T in triacetin.
5. 8% Hydrogen Peroxide.

If, therefore, a vesicant attack is launched and if for any reason military personnel are unable to adequately perform immediate personal decontamination, they may receive same at medical installations both mobile and fixed. In addition civilians may be treated at fixed medical installations.

If a vesicant gas attack takes place, Medical Department personnel will effect personal decontamination, change clothes if indicated and those who are to handle casualties will don protective clothing, gas mask and apply protective ointment.

In this Theater of Operations the handling of vesicant casualties in Fixed Medical Installations is covered by a letter, Office of the Chief Surgeon, 22 May 1943. In brief, the present policies here are:

1. Early sorting of casualties into:

   a. Wounded contaminated.
   b. Wounded non-contaminated.
   c. Non-wounded contaminated.

2. Wards are previously designated for handling these cases.

3. Decentralization of treatment areas. Use of ward corridor to decontaminate and reclothe patients. Thereafterpatients are sent to the ward.

4. Contaminated clothes and valuables storedin impervious paper bags and later decontaminated or disposed of.

5. Wounded contaminated will be treated first from the point of view of the surgical condition present and secondarily from the point of view of the vesicant. Thus, if indicated such cases will be taken directly to the operating room and the surgical condition treated. Vesicant decontamination will be performed during or after the operation.

6. Gas casualty treatment supplies will be available at all treatment points.

Occasionally liquid lacrimators and particulate smokes will cause injury when the agent comes in contact with the skin. First aid for these agents is to flush the skin with large amounts of water.

First aid for White Phosphorus burns is to immediately apply wet cloths to the area. Copper sulfate 5 to 10% can be applied and then the pieces of white phosphorus are manually removed from the skin.

Definitive Treatment:

Definitive treatment for vesicant casualties is the same regardless of the

responsible agent, i.e., it is dermatologic treatment directed to the appearance of the eruption. For the sake of convenience in the following discussion, cases will be divided into ambulatory and hospitalized and, furthermore, lesions near the eyes and on the genitals will be separated from those on the rest of the body.

A. Ambulatory cases, i.e., burns are not extensive or involving vital area. No interference with carrying out routine duties.

I. Stage of erythema, edema, and subjective symptoms.

a. Mustard.

PRESCRIPTION NO. (1) Calamine lotion with ¼ to ½% menthol or phenol.

b. Lewisite

1. Lotion as above.

(2) 2. Hydrogen peroxide 8% may be used. It will do no harm and it may oxidize some of the trivalent arsenic still present and thereby prevent greater injury. Do not use in eyes or allow to enter eyes.

II. Blistering Stage.

a. Lesions near eyes and on genitals.

1. Evacuate large, tense blisters by inserting a sterile hypodermic needle in dependent portion of blister after first sterilizing skin with alcohol. Do not denude blisters.

(3) 2. Lassar's Paste.

(4) 3. Boric acid ointment.

(5) 4. Zinc oxide ointment.

(6) 5. Sulfadiazine ointment if evidence of secondary infection is present.

6. Dry dressings in healing stage.

b. Lesions on trunk and extremities.

(7) 1. Amyl Salicylate wet dressings. Apply the amyl salicylate to gauze and apply this to the lesion. Keep the dressings moist with the remedy until healing begins.

2. Prescriptions No. (3), (4), (5) and (6) can also be used.

B. Severely burned hospitalized cases. Extensive lesions interfering with carrying on duties.

I. Stage of erythema.

a. May use prescriptions No. (1) and (2).

b. In addition:

1. Wet Dressings (cold).

PRESCRIPTION NO.

a. Near eyes or on genitals.

(8) 1. Saturated boric acid solution.
(9) 2. Physiological saline solution
(10) 3. Aluminum acetate or subacetate 1:10 or 1:20.

b. On trunk and extremities:

1. Same as above. In addition:
(11) 2. Potassium permanganate solution: 1:5000 to 1:10,000
(12) 3. Menthol ¼%, alcohol 25%, saturated boric acid solution q.s.
(13) 4. Alcohol 25 to 50%.

2. Lotions: Shake lotion, base may consist of the following: zinc oxide, talc, prepared calamine. One or all of the above to total 30 or 40 grams in 120 c.c. of lotion. Sample lotion:

(14)

Zinc oxide		
Talc	aa	15.0 or 20.0
Glycerine		10.0
Water	q.s. ad	120.0

or

(15)

Prepared calamine		
Zinc oxide	aa	15.0 or 20.0
Glycerine		10.0
Water or lime water	q.s. ad	120.0

Lotions can be used on all body areas with care. Anti-pruritic adjuvants to the above lotions:

(16) a. Menthol ¼ to ½%
(17) b. Phenol ¼ to ½%
(18) c. Liquor carbonis detergens 1 to 5%

(19) 3. Tinctures: To be used only on trunk and extremities. Base is alcohol or alcohol and ether, plus the following:

a. Menthol ¼ to ½%
b. Camphor ½ to 2%

4. Pastes: Base may be usual Lassar's base made with zinc oxide and starch, or the following base:

(20)

Zinc oxide		.0
Talc	aa	25.0
Vaseline	q.s. ad	100.0

PRESCRIPTION NO.

May be used plain or with antipruritic adjuvants listed under lotions above.

5. Medicated baths: Are indicated in more or less generalized cases or where itching and pain is intolerable. Are given lukewarm, from 15 minutes to an hour. It must never be given hot. Can be repeated as indicated. The following can be added:

(21) a. Oatmeal gruel tied up in a cloth bag and "swished" around in the water.

(22) b. Bran ½ to 1 lb. tied up in a cloth bag and "swished" around in the water.

(23) c. Starch ½ to 1 lb. Mix starch with sufficient cold water to make a thin suspension. Pour this slowly into boiling water, stirring vigorously. Pour resultant paste into bath water.

(24) d. Potassium permanganate 1:10,000 to 1:20,000.

(25) e. Several cups of liquor carbonis detergens added to the water. (For itching).

6. Ointments: Prescriptions No. (3), (4), (5), (6) can be used. In the erythema stage, however, ointments are usually contra-indicated.

II. Stage of Blistering:

a. Near eyes or on genitals:

1. Prescriptions No. (8), (9), and (10) can be used.
2. Lotions No. (14) or (15) plus adjuvants No. (16), (17) and (18) may be used.
3. Baths No. (21), (22), (23), (24) or (25) can be used.

b. On trunk and extremities:

1. Amyl salicylate as in (7).
2. Ointments and pastes listed under (3), (4), (5) and (6).
3. Lotions and baths and wet dressings listed under (1), (2), (8), (9), (10), (11), (12), (13), (14), (15), (16), (17), (18), (21), (22), (23), (24), and (25).

Blisters should preferably not be denuded. If the blisters are tense, they may be evacuated by means of a sterile needle puncture in the dependent portion after first sterilizing the skin with alcohol.

III. Stage of Healing:

a. Dry dressings.
b. Lotions (14) or (15) plus adjuvants (16), (17) or (18).

c. Pastes and ointments listed in (20), (3), (4), (5), and (6).

(26) d. Calamine liniment.

IV Secondary infection:

a. Near eyes:

(27) 1. Use a sulfonamide ophthalmic ointment (none standardized as yet). Do not use a sulfonamide skin ointment near eyes. In general avoid prolonged use of sulfonamide ointments. Do not use these ointments on large denuded areas because of the danger of quantitative absorption.

b. On genitals, trunk and extremities:

(28) 1. Sulfadiazine ointment (See precautions noted in prescription No. (27) above).

2. Prescription No. (11) may be used.

(29) 3. Wet dressings of silver nitrate $\frac{1}{4}$ to $\frac{1}{2}$%.

Treatment of Thermite and White Phosphorus Burns: After the active agent has been removed, the treatment is the same as for thermal burns of similar degree.

TECHNIC OF DERMATOLOGIC MEDICATION

It is well known that a certain remedy will have no effect on a certain dermatosis at one time, yet at another time will have beneficial effects. One of the probable reasons for this is that at one time the remedy may be "slapped on", while at another time it may be properly applied and removed. The proper removal of remedies is as important as proper application. It is better not to treat than to treat and increase injury. An old dermatologic maxim is: "The proper remedy is the one which can be properly applied, properly removed and worn constantly". Thus, whenever possible lotions should be used on the trunk, rather than ointments, because the latter wipe off, must be bandaged and in general are messy and uncomfortable on this area.

Wet Dressings: These are especially suited for acute, edematous, erythematous, oozing dermatoses. The cloth used should preferably be soft (never gauze), e.g., old sheets, pillowcases etc. Two methods of application are available:

1. Dressings are dipped into the solution and applied. This is repeated every 15 minutes to one-half hour.
2. Dressings are bandaged on the part and solution is sprayed on the dressings with a syringe at frequent intervals.

Wet dressings used in acute dermatoses must never be allowed to dry out. If they do, they are worse than no treatment and are usually violently irritating.

The solution should be cold and kept available at the bedside. The bandages must never be covered with impervious material since the beneficial effect of wet dressings is dependent on evaporation at the surface of the dressing.

Medicated Baths: The bath water should be tepid. The bath must never be hot. The patient may remain in the bath from 15 minutes to hours. As the water cools hot water is added to maintain the tepid temperature. Baths are especially indicated in acute, erythematous, itching, oozing dermatoses. They are particularly useful at night to cause "relaxation" and promote sleep. The patient after the bath is patted, never rubbed dry. The remedy in use at the time (whether lotion, paste, etc.) is immediately reapplied after the bath.

Shake Lotions: These are useful in acute and subacute dermatoses. They are best applied with a small varnish brush. The bottles in which lotions are dispensed should be of the wide-mouth type to permit insertion of the paint brush. One layer of lotion is applied on top of the other. When "caking" occurs it is gently washed off with saline or boric acid solution and fresh lotion is immediatly reapplied. The area is cleansed gently twice daily, or if baths are permissable, the area is gently cleansed in the bath. Lotions should be reapplied:

1. If the old application is brushed off.
2. Whenever symptoms (itching, burning etc.) are present. There is usually no limit to the frequency or number of applications. The only important consideration is that the involved area must always be covered by the remedy. Lesions treated with lotions are not bandaged.

Tinctures: What was said for lotions applies to tinctures, except that they may be applied with cotton.

Ointments and Pastes: These are indicated in subacute or chronic dermatoses. In acute dermatoses itching and other sensory disturbances may be aggravated by the heating effect of ointments because they interfere with heat loss. Heat loss is particularly desirable in acute dermatoses because it is said to cause vascular constriction.

Pastes are indicated where secretions are present, since the latter can seep through the porous past but cannot do so through the relatively impervious ointment.

Ointments and pastes should always be bandaged on, except on the face. On the face they are not easily brushed off. Ointments are applied directly to the lesions in thick layers. A soft piece of cloth (old sheet etc) is also buttered with the ointment and applied over the involved area. This may then be covered with gauze bandage. The gauze must not, however, touch the inflammed skin. These medicaments are removed by gentle cleansing with wads of cotton saturated with mineral or vegetable oil, and fresh ointment or paste is immediately reapplied.

General Hints:

Menthol is cooling. When a lotion or tincutre contains menthol, apply to

small areas and allow the remedy to dry, before applying to other areas. If this precaution is not observed the patient may have a "chill".

Protection from air usually reduces itching. Therefore, lesions should be constantly covered by the medicament in use.

Soap is usually not well tolerated in acute dermatoses, in fact in all inflammatory skin lesions whether acute or chronic. Cleanse areas with boric acid solution, saline or plain water rather than soap.

Occasionally a remedy may arravate existing symptoms. The most frequent cause is sensitivity to the remedy. Stop the remedy being used and substitute another.

General Measures:

During the itching stage and during the blistering stage, sedatives and analgesics are valuable. If much serum is lost during the blistering stage, consider the use of fluids, plasma and whole blood transfusions. In the stage of recovery anemia, anorexia, etc. can be combatted by general supportive measures as: high-vitamine-high-caloric diet, liver and iron medication.

Surgical Measures:

If ulceration or secondary infection has caused scarring, plastic surgery must be considered if the scar is on the face or neck or if it interferes with movement of a joint or vital part. Early passive and active movements of scarred joints is indicated.

Complications of Treatment:

The main complication of treatment is dermatitis from Protective Ointment. With M-4 Ointment this is usually not serious, reactions are superficial and subsi promptly when the ointment is discontinued. M-4 Ointment does not sensitize the individual to subsequent applications. In addition to the dermatitis from Protective Ointment, contact dermatitis from other medicaments locally applied may occur. This is treated by substituting another remedy for the one causing the dermatitis.

PSYCHOLOGICAL ASPECTS

The psychological aspects of Chemical Warfare in general, and vesicant effects specifically, are important from the practical point of view. The more proficient in training, in protection, first aid and treatment of vesicant effects, the less liklihood there is that casualties will be excessive or that such attack will be demoralizing. Here "knowledge is power" really applies. Knowledge of the methods of dispersal, the effects and available methods of combating such effects creates a feeling of confidence. Each soldier should be made to feel

that a vesicant attack is an annoyance, rather than a lethal weapon. Deaths from dermatologic effects and even general effects from vesicants in World War I were very low. Complications under modern methods of treatment should be practically non-existent. Sequelae other than increased sensitivity to mustard are rare. Sequelae are mainly psychological. All military personnel and all civilians must know these facts.

It is the conviction of some that combat units should be exposed to actual chemical agents during their training. It is said that such exposure brings home to the individual soldier that eternal vigilence and intensive training pays dividends. Under such actual warfare conditions only negligent individuals will become casualties and even these in most cases will be able to carry on and take the results of such negligence in their stride. Instead of babying such cases and hospitalizing all of them as was the practice in World War I, a much more practical attitude should be the rule. Unless the injury to the skin is more or less generalized or in such a location as to interfere with locomation or handling a weapon, the individual is no longer assessed as a casualty.

The question of sensitization of troops exposed to mustard during such training with actual agents must be considered. It is difficult to decide which of the following is preferable:

1. To have well trained troops who have been exposed to mustard and are not afraid of it, but who because of sensitization become casualties on first exposure to even small quantities of the agent.

2. To have troops who have not been trained with the actual agent who will fear the agent, but who will not become severe casualties on first exposure.

Which of the above is preferable is still being debated.

The Royal Canadian Army Medical Corps classifies vesicant injuries as follows:

Class I. A casualty under any circumstance, regardless of how willing the man is to continue his duties, or how acute the situation. Mobility of one or more limbs is seriously impaired.

Class II. The state sometimes referred to as "Just not a casualty".

a. Mobility of one or more limbs is limited but not completely impeded by lesions in their full maturity. The man would become a casualty if required to do any work involving strenuous exercise such as running $\frac{1}{2}$ mile or marching 2 miles.

b. The extent or position of the lesions prevent the application of a dressing which would remain in position during strenuous exercise. Lesions involving the sensitive areas often fall into this class.

For purposes of assessment, these classes are in the casualty group.

Class III. Not a casualty, although the burns may be prominent and several in number. The mobility of the limbs is not interfered with and is unlikely to be interfered with even on strenuous exercise.

Class IV. Not a casualty. Trivial and insignificant burns.

For purposes of assessment, these classes are in the Non-Casualty group.

MISCELLANEOUS

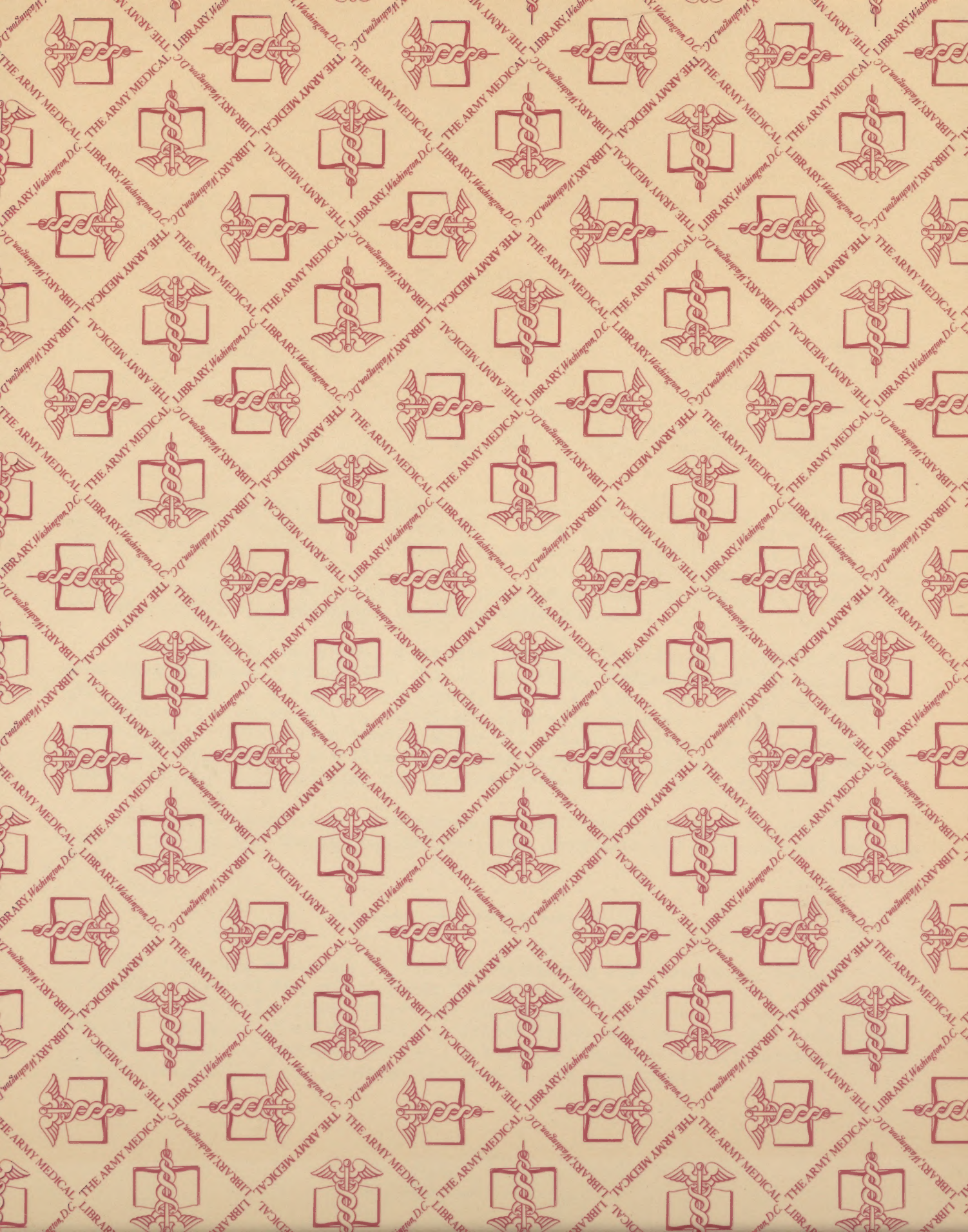
Dermatitis from Rubber of Gas Mask Face Piece: Instances of such dermatitis are occasionally reported. They are usually due to the usual causes of rubber dermatitis, i.e., accelerators and antioxidants. The localization on the face, the history, and application of proper patch tests will usually make the diagnosis. This condition is rarely met with in personnel who wear United States Army gas masks, because the rubber chosen for the mask is carefully tested to avoid such reactions in so far as is possible.

Industrial Hazards: Industrial skin hazards are frequent in factories manufacturing Chemical Warfare materials. These vary from the primary irritant effects of the ingredients of chemical agents to the specific effects of the finished product, e.g., mustard, lewisite. Skin burns of varying degree are constantly observed in the personnel of such places and give the research medical officer excellent opportunities for therapeutic research.

In addition to the above, dermatitis from the ingredients of ointments, protective clothing, impregnites, rubber, plastics, synthetics, cloth, metals, dyes, paints, oils, lacquers, detergents, solvents, etc., etc. Some of these dermatidites are non-specific, others are typically allergic. A careful history, application of proper patch tests and careful clinical evaluation will usually aid in the diagnosis. A follicular, non-allergic inflammatory dermatitis has been observed in personnel handling rubber cloth protected by finely ground mica.

The solvent used in the impregnation of protective clothing is said to be absorbed through the intact skin and can cause hepatitis and even acute yellow atrophy of the liver.

The foregoing monograph is intended to clarify for certain key Medical Department personnel the relationship between vesicant agents and the skin. Physicians in civilian practice are not experienced in the care of cases of this sort and it is hoped that the matter contained herein will relieve this deficiency. Upon the outbreak of Chemical Warfare, the Medical Department will naturally assume the responsibility of the professional care of gas casualties.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